

U.S. Patent Appln. S.N. 09/847,384
AMENDMENT AFTER FINAL REJECTION

PATENT

IN THE CLAIMS:

Please cancel claim 33 without prejudice or disclaimer, rewrite claims 34-36, 38, 40, 41, 46, 48 and 50, and add new claim 51, as shown below in the detailed listing of all claims which were, or are, in the application:

Claims 1-33 (Canceled)

34. (Currently amended) The labeling reactant of ~~claim 33~~ claim 51, wherein R is a member of the group consisting of 4,4'-dimethoxytrityl, 4-methoxytrityl, trityl, and (9-phenyl)xanthen-9-yl.

35. (Currently amended) The labeling reactant of ~~claim 33~~ claim 51, wherein X" is a member of the group consisting of t-butyltrimethylsilyl-, tetrahydropyranyl, 1-(2-fluorophenyl)-4-methoxypiperidin-4-yl-, 1-[2-chloro-4-methylphenyl]-4-methoxypiperidin-4-yl-, 4-methoxytetrahydropyran-4-yl-, phthaloyl-, acetyl, pivaloyl-, benzoyl-, 4-methylbenzoyl, benzyl-, and trityl.

36. (Currently amended) The labeling reactant of ~~claim 33~~ claim 51, wherein G is a protected functional group.

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37. (Previously presented) The labeling reactant of claim 36, wherein said protected functional group is selected from the group consisting of amino, carboxyl, aminooxy and thiol.

38. (Currently amended) The labeling reactant of ~~claim 33~~ claim 51, wherein G is an organic dye.

39. (Previously presented) The labeling reactant of claim 38, wherein said organic dye is selected from the group consisting of dabsyl, dansyl, fluorescein, rhodamine and tetramethyl-6-carboxyrhodamine (TAMRA).

40. (Currently amended) The labeling reactant of ~~claim 33~~ claim 51, wherein the temporary protecting group R is 4,4'-dimethoxytrityl.

41. (Currently amended) The labeling reactant of ~~claim 33~~ claim 51, wherein said reactant is a nucleotide and the sugar of the nucleotide is 2-deoxyribose or 3-deoxyribose.

42. (Previously presented) The labeling reactant of claim 41, wherein X' is hydroxyl.

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43. (Previously presented) The labeling reactant of claim 42, wherein the permanent protection group X" of X' is selected from the group consisting of t-butyldimethylsilyl, tetrahydropyranyl, 1-(2-fluorophenyl)-4-methoxypiperidin-4-yl-, 1-[2-chloro-4-methyl)phenyl]-4-methoxypiperidin-4-yl- and 4-methoxytetrahydropyran-4-yl-.

44. (Previously presented) The labeling reactant of claim 41, wherein X" is an alkyl or alkoxyalkyl.

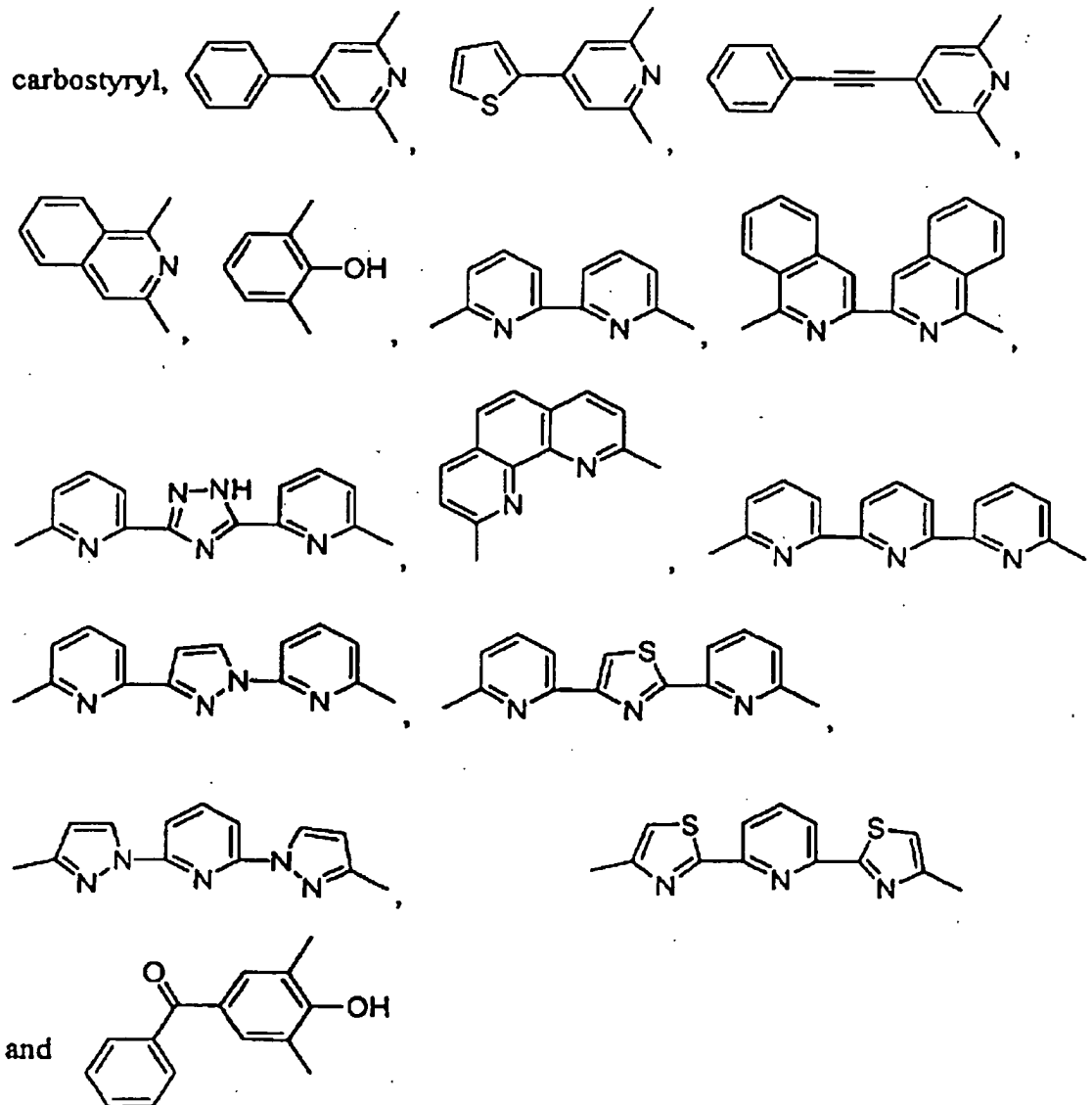
45. (Previously presented) The labeling reactant of claim 44, wherein X" is selected from the group consisting of methyl, methoxymethyl and ethoxymethyl.

46. (Currently amended) The labeling reactant of ~~claim 33~~ claim 51, wherein G is a bivalent aromatic structure.

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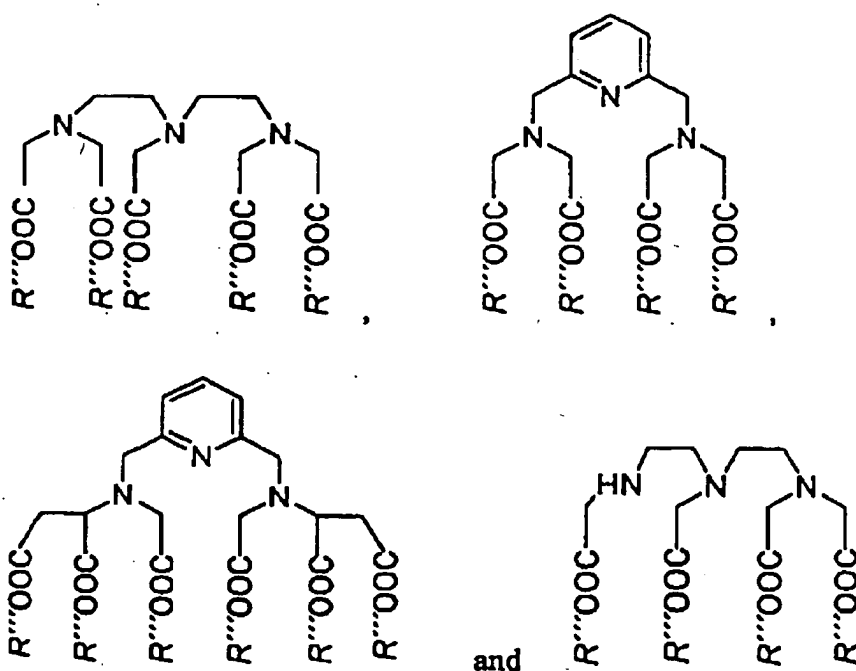
47. (Previously presented) The labeling reactant of claim 46,
wherein G is selected from the group consisting of



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48. (Currently amended) The labeling reactant of ~~claim 33~~ claim 51, wherein said reactant is non-luminescent and G is selected from a group consisting of



and wherein

R''' is an alkyl of 1 to 4 carbon atoms, allyl, ethyltrimethylsilyl, phenyl or benzyl, which phenyl or benzyl can be substituted or unsubstituted, and one of the hydrogen atoms is substituted with E'.

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49. (Previously presented) The labeling reactant of claim 48, wherein R'' is selected from the group consisting of methyl, ethyl and allyl.

50. (Currently amended) The labeling reactant of ~~claim 33~~ claim 51, wherein the labeling reactant is selected from the group consisting of

2'-deoxy-5'-O-(4,4'-dimethoxytrityl)-N3 {tetramethyl 2,2',2'',2'''-[(4-(1-hexyn-5-yl)pyridine-2,6-diyl)bis(methylenenitrilo)]tetrakis(acetato) uridine 3'-O-(2-cyanoethyl N,N-diisopropyl) phosphoramidite,

N3-[6-[4-(dimethylamino)azobenzene-4'-sulfonamido]hex-1-yl-5'-O-(4,4'-dimethoxytrityl)thymidine 3'-O-(2-cyanoethyl N,N-diisopropyl) phosphoramidite,

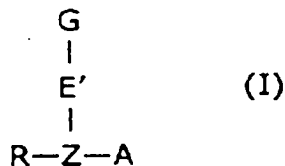
5'-O-(4,4'-dimethoxytrityl)-N3-{tetramethyl-2,2',2'',2'''-{6,6'-[4'-hydroxyethoxyethoxyphenylethynyl]pyridine-2,6-diyl)bis(methylenenitrilo)tetrakis(acetato)}thymidine 3'-O-(2-cyanoethyl N,N-diisopropyl) phosphoramidite, and

2'-deoxy-5'-O-(4,4'-dimethoxytrityl)-3-6-{{4-(6,6''-bis[N,N-bis(methoxycarbonylmethyl)aminomethyl]-2,2':6',2''-terpyridine-4'-yl}phenyl}hex-5-yn-1-yl}uridine 3'-[O-(2-cyanoethyl)-N,N-diisopropyl]phosphoramidite.

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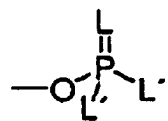
51. (New) A labeling reactant of formula (I) suitable for labeling an oligonucleotide



wherein

R is a protecting group or is hydrogen;

A is either a phosphorylating moiety



where

L is O, S, or is not present

L' is H, L''CH₂CH₂CN or L''Ar, where Ar is phenyl or its substituted derivative, where the substituent is nitro or chlorine, and L'' is O or S;

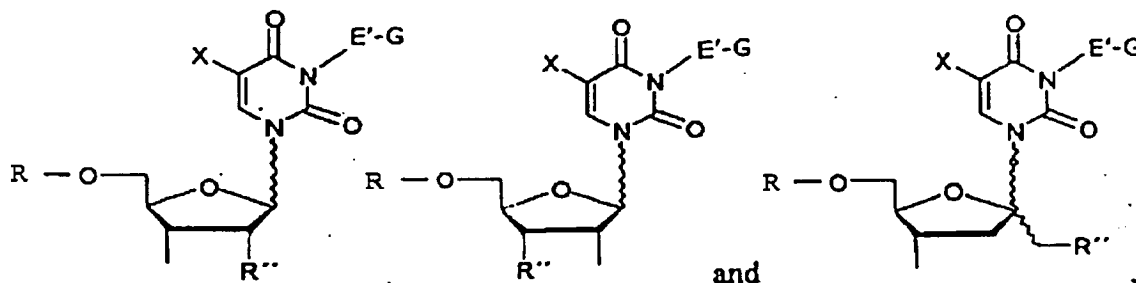
L'' is O⁻, S⁻, Cl, N(i-Pr)₂; or

A is a solid support tethered to Z via a linker arm, which is formed of one to ten moieties, each moiety being selected from a group consisting of phenylene, alkylene containing 1-12 carbon atoms, ethynediyl, ether, thioether, amide, carbonyl, ester, disulfide, diaza, and tertiary amine;

Z is a bridge point and is formed from

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where

R'' is H or X'X'', where

X' is -O-, -S-, -N-, ON- or -NH- and X'' is a protection group or

X' is -O- and X'' is alkyl or alkoxyalkyl;

X is H, alkyl, alkynyl, allyl, Cl, Br, I, F, S, O, NHCOCH(CH₃)₂, NHCOCH₃, NHCOPh, SPh₂, OCOCH₃, or OCOPh;

E' is a linker arm between G and Z, bonded to Z at nitrogen in the pyrimidyl ring and is formed of one to ten moieties, each moiety being selected from the group consisting of phenylene, alkylene containing 1-12 carbon atoms, ethynediyl, ether, thioether, amide, carbonyl, ester, disulfide, diaza, and tertiary amine, or is not present;

G is a bivalent aromatic structure, tethered to two iminodiacetic

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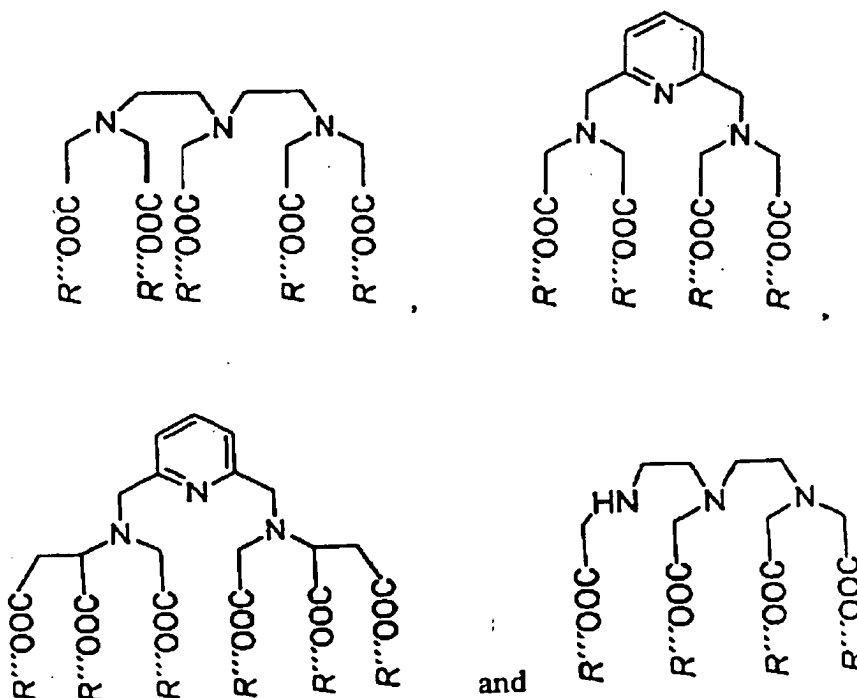
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acid ester groups $N(CH_2COOR'')$, where

R'' is an alkyl of 1 to 4 carbon atoms, allyl, ethyltrimethylsilyl, phenyl or benzyl, and

said bivalent aromatic structure is capable of absorbing light or energy and transferring the excitation energy to a lanthanide ion after the solid phase synthesis made labeling reactant has been released from the used solid support, deprotected and converted to a lanthanide chelate, or

G is a structure selected from a group consisting of



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where

R'' is an alkyl of 1 to 4 carbon atoms, allyl, ethyltrimethylsilyl, phenyl or benzyl, and

one of the hydrogen atoms is substituted with E', or

G is a protected functional group, where the functional group is amino, aminooxy, carboxyl, thiol, and the protecting group is phthaloyl, trityl, 2-(4-nitrophenylsulfonyl)ethoxycarbonyl, fluorenylmethyloxycarbonyl, benzyloxycarbonyl, trifluoroacetyl or t-butoxycarbonyl for amino and aminooxy, alkyl for carbonyl and alkyl or trityl for thiol.